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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,946	04/19/2001	L. David Williams	MVIEWD.1A2DV1	5256

26111 7590 03/05/2004

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EXAMINER

SAIDHA, TEKCHAND

ART UNIT PAPER NUMBER

1652

DATE MAILED: 03/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/839,946	WILLIAMS ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Tekchand Saidha	1652	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 50-59 and 74-76 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 50-59 and 74-76 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

### Final Rejection

1. Applicant's arguments filed 1.23.2004 have been considered and not found to be persuasive. The reasons are discussed following the rejection(s).
2. Any objection or rejection of record which is not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.
3. At the Examiner's telephone request on February 26, 2004, Applicants' provided copies of Information disclosure statements and references filed December 11, 2003; December 16, 2003; January 23, 2004 (after the first Office Action on the merits) which is very much appreciated and acknowledged. Signed copies of Form PTO-1449 are enclosed.
4. Also during the telephone interview on February 26, 2004, the Applicants' representative, Brian J. Del Buono requested a signed copy of the prior IDS, filed September 25, 2001. A signed copy of this is enclosed.
5. Examiner's indication of allowability of claims 50-59 and 74-76 to Mr. Brian Buono, on 02.26.2004 is withdrawn. Having reconsidered the claim language in the light of the art cited as well as the filing of new information disclosure statements, this verbal allowability of the pending claims is withdrawn.

6. Claims 1-49 & 60-73 have been cancelled by Applicants' amendment filed 1.23.04.

7. Claims 50-59 & 74-76 drawn to an isolated tetrameric mammalian uricase are pending and under consideration in this Office Action.

8. *Claim Rejections - 35 U.S.C. § 112* (second paragraph)

Claims 50-59 & 74-76 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 50, line 2, recites the phrase 'contains no more than about 10% non-tetrameric'. The phrase is vague and indefinite because the specification does not define the meaning of 'non-tetrameric' and which is not a well defined or art accepted phrase and one of skill in the art would not understand the meets and bounds of the claim. What is the nature of the 'non-tetrameric material' ? Does it mean the presence of impurities of any kind to the tune of no more than 10%; which may mean that impurities in the preparation can be any material which is not tetrameric, or which may be any other compound or protein or material; and contain *up to* 10% impurities.

Claims 51-59 & 74-76 are included in this rejection for failing to correct the defect present in the base claim(s).

9. *Claim Rejections - 35 U.S.C. § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 50-53 and 74-76 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Cheng et al. [Science 239, 1288-1291 (1988)], or Wu et al. [PNAS, USA, Vol. 86, pp. 9412-9416, December 1989].

The rejection is being made under 102/103, because protein aggregation is an intrinsic property of the protein and is depended upon the concentration of the protein in solution. The aggregation of a purified uricase preparation can be varied by

varying the protein concentration in solution, thereby achieving 10% or a desired level of aggregation of non-tetrameric uricase.

Cheng et al. (1988) teach the recombinant production of full length amino acid sequence of porcine Urate oxidase (uricase) which is tetrameric and is substantially pure. Mammalian uricase is disclosed as a tetramer with subunit size of 32,000 daltons (page 1288, column 2, first paragraph after the abstract). The reference further teaches purification to homogeneity of Porcine and murine urate oxidase (see, page 1289, second column). Oxidation of uric acid to allantoin is catalyzed by urate oxidase (see abstract). Increased uric acid level, due to lack of this enzyme in man can lead to gouty arthritis (page 1288, column 2).

Wu et al. teach recombinant production and sequencing of urate oxidase or uricase from baboon, mouse and pig (porcine) [See figure 1]. Mammalian uricases are taught to tetramers (see page 9412, column 1). The uricase can be recombinantly expressed and purified and the percent of non-tetrameric aggregates varied as indicated above.

Protein aggregation being the intrinsic property of the protein, it would have been obvious for one of ordinary skill in the art to vary the aggregation percent by varying the purified protein(s) [cheng et al (1988) or Wu et al.] concentration by

what is well known in the art of protein chemistry as exemplified in the works of Malakhova et al. [see the following abstract in item 9(a)] and to develop suitable pharmaceutical compositions for parenteral administration or inhalation, knowing from the teachings of cheng et al (1988) or Wu et al. that uricase is involved in lowering uric acid levels in body fluid or tissue.

Applicants' arguments :

Applicants citing page 16, lines 5-16 of the instant specification, argue that purified preparations of natural or recombinant uricase contain a mixtures of aggregates of the enzyme, in addition to the tetrameric form, and the non-tetrameric form varies from 10%-80%, and that Chen's preparation will contain substantial quantities of more than 10% of non-tetrameric form of the enzyme.

However, Applicants' specification on page 16, line 9, gives a range of 20%-90%, and further Applicants' have no basis in stating that cheng's preparation will have more than 10% of non-tetrameric form of the polypeptide.

Further, as noted above, protein aggregation is an intrinsic property of the protein, and therefore obvious for one of ordinary skill in the art to vary the aggregation percent by varying the protein concentration [for example : see Malakhova

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et al. Biologicheskije Membrany (1991), 8 (5), 453-9, abstract is provided here] and to develop suitable pharmaceutical compositions for parenteral administration or inhalation, knowing that uricase is involved in lowering uric acid levels in body fluid or tissue.

9(a) ABSTRACT

TITLE: Kinetic properties of bacterial urate oxidase entrapped in hydrated reversed micelles

AUTHOR(S): Malakhova, E. A.; Chebotareva, N. A.; Kurganov, B. I.; Simonyan, A. L.

CORPORATE SOURCE: All-Union Vitam. Res. Inst., Moscow, USSR

SOURCE: Biologicheskije Membrany (1991), 8(5), 453-9

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB The kinetics of the enzymic reaction catalyzed by urate oxidase from *Bacillus fastidiosus* entrapped in Aerosol OT hydrated reversed micelles in octane were studied. The value of the maximal rate of the enzymic reaction ( $V$ ) remained virtually constant as the degree of reversed micelle hydration ( $[H_2O]/[AOT] = w_0$ ) increased from 7.4 to the value at which the dimensions of the micellar internal cavity coincided with those of the enzyme mol. ( $w_0 < 23$ ). At  $w_0 > 30$  the maximal rate of the enzymic reaction was observed to rise unexpectedly. The results of sedimentation expts. on reversed micelles suggest the unusual character of the dependence of  $V$  on  $w_0$  to be due to enzyme aggregation in reversed micelles. The observed decrease of the apparent Michaelis constant with the decrease in  $w_0$  is associated with the local concentration of the substrate in the water phase of reversed micelles.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is

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reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

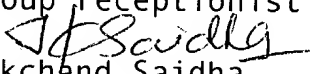
A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (571) 272-0940. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (571) 272-0928. The fax phone number for this Group in the Technology Center is 703 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 571 272-1600.

  
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February 24, 2004  
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